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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,697	01/30/2002	Donald W. Petersen	06317-038003	8553

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ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER

WITZ, JEAN C

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/060,697

Applicant(s)

PETERSEN, DONALD W.

Examiner

Jean C. Witz

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>04/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 2, 2004 has been entered.

Response to Arguments

Applicant's arguments filed April 2, 2004 have been fully considered but they are not persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 16-30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of O'Leary et al. (5,484,601), Yim et al. and WO 9840113 taken as a whole.

Applicants assert that the teaching of the Yim reference to include calcium sulfate hemihydrate in a bone graft formulation must be limited to the formulation of U.S. Patent 5,171,579, and therefore, there is no motivation to include it in the composition of O'Leary et al. Applicants also appear to be repeating an argument made previously that the inclusion of calcium sulfate of Yim into the composition of O'Leary is not necessary (and therefore not motivated) since "the O'Leary patent seems to suggest that the consistency of the 'flowable' material can be adjusted simply by altering the amount of the liquid component (column 3, lines 28-35). In the previous office action, Applicant asserted that the "reasons for adding calcium sulfate are either inconsistent with the type of compositions that O'Leary intended to form or have already been addressed by O'Leary."

Yim specifically teaches that "[t]o reduce the preparation time and improve the above formulation's handling characteristics, [Patentees] have surprisingly found that it is desirable to add a calcium sulfate hemihydrate-containing substance (CSHS). The CSHS is preferably either pure calcium sulfate hemihydrate, also known as Plaster of Paris (POP), or a mixture of POP and hydroxyapatite (POP:HA). Adding a CSHS reduces setup time and provides improved moldability and consistency of the resulting formulation." Applicants states that "Yim only suggests a CSHS provides such advantages in the context of a formulation comprising osteogenic proteins, autogenous blood, and a porous particulate polymer matrix, such as a copolymer of lactic acid and glycolic acid (PLGA)." This argument is not persuasive since Applicants do not address that the "above formulation" discussed by Yim supra includes a suitable

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“protein-sequestering agent”, disclosed at col. 7, lines 25-34, as cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), such as methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose. Yim already includes the thickener of O’Leary yet finds that the addition of calcium sulfate improves the composition for certain applications . As a result, one of ordinary skill in the art would expect the composition of O’Leary would similarly be improved for certain applications by the inclusion of calcium sulfate, as one of ordinary skill in the art would also expect that the composition of O’Leary would be improved for certain applications by the inclusion of the cancellous bone disclosed by Wironen.

With regard to the suggestion that O’Leary requires only that the “consistency of the ‘flowable’ material can be adjusted simply by altering the amount of the liquid component”, Applicants do not take into consideration that O’Leary envisions a range of consistencies of the composition and defines “the term ‘flowable’ as used herein applies to compositions whose consistencies range from those which can be described as shape-sustaining but readily deformable, e.g., those which behave like putty, to those which are runny. Specific forms of flowable bone powder compositions include cakes, pastes, creams and fillers.” O’Leary et al. state at col. 1, lines 36-43 that “[I]t is a particular object of the invention to provide a composition of liquid or pastelike consistency comprising demineralized osteogenic bone powder and a biocompatible liquid synthetic organic material as a carrier for the bone powder with or without such

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optional ingredients as thixotropic agents, medicaments, and the like, and to apply the composition at a bone defect site to induce new bone ingrowth at the site.”

Therefore the goal of the invention is to provide a composition that is a carrier for the demineralized bone powder as well as other optional ingredients and one that has a myriad of different consistencies to fulfill the requirements of the specific use.

O’Leary et al. disclose at col. 2, line 53 to col. 3, line 13, that “[a]ny of a variety of substances can be introduced into the bone particles” and includes a non-limiting list which includes inorganic elements, parenchymal cells, growth factors, bone morphogenic proteins, and mesenchymal elements. “ (emphasis added.) Calcium sulfate would be considered by one of ordinary skill in the art to be such an “inorganic element”.

This is an express statement of O’Leary of motivation to combine other ingredients as necessary and required and this list of ingredients is clearly broad in scope and non-limiting in nature. With regard to this teaching, Applicants mere state that “[s]uch a general teaching really has no bearing at all on the specific question of whether one of ordinary skill in the art would have been motivated to combine the calcium sulfate hemihydrate teaching of Yim with the formulation in O’Leary.” This is statement provides no evidence and an unsupported conclusion. Applicants further argue (addressing the statement by the Examiner that “the Yim and O’Leary formulations are ‘sufficiently similar’ such that one of ordinary skill would be aware that calcium sulfate hemihydrate ‘would not impair or otherwise negatively affect’ the O’Leary composition) that “the simple understanding by one of ordinary skill in the art

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that the addition of a certain compound to a composition would not negatively affect that composition is insufficient to motivate one to make such a combination. The art must provide a positive motivation to make the combination suggested in the rejection rather than simply fail to teach against such a combination.” This argument is not persuasive because the statements of the Examiner are not the only basis for motivation and merely point out that there is no explicit or implicit teaching that directs one of ordinary skill away from adding calcium sulfate hemihydrate to the composition of O’Leary.

Similarly, Applicants argue that the teaching of Wironen regarding the inclusion of cancellous bone must be limited to cross-linked gelatin based formulations. This is also similar to arguments made in previous responses. Applicants’ piecemeal analysis fails to address the teaching of the references taken as a whole. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Examiner pointed out in the previous office action that the disclosure of WO 9840113 is also drawn to a bone paste for the repair of bone defects. The disclosed paste contains demineralized bone matrix, an inorganic component such as ceramics hydroxyapatite and calcined bone, or bone morphogenic proteins or other growth factors and mixtures thereof. Other ingredients which may be present in the paste include wetting agents and carboxymethyl cellulose (see pages 5-6). At page 13, the reference states that the composition “may act as a carrier for cortical, cancellous or cortical and cancellous bone chips. Such compositions are useful for filling larger bone voids. In addition, when these bone chips are not

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demineralized, they provide an added spectrum of biological properties not exhibited by the gelatin alone or the gelatin plus the osteogenic components (i-iv).” Therefore, the disclosure of Wironen specifically teaches one of ordinary skill in the art that there is a motivation to include cancellous bone into a bone repair composition for the reasons set forth above. Applicants arguments that the disclosure of Wironen must be interpreted to mean that cancellous bone can only be included in the composition of Wironen unpersuasive because that interpretation is too limited. One of ordinary skill in the art, in view of the teachings of Wironen, would be aware that the benefits that the cancellous bone brings to the composition of Wironen would be expected by one of ordinary skill in the art to accrue to other bone repair compositions. O’Leary, Yim and even Wironen himself provide disclosures such as found in virtually every patent document as exemplified at page 6 of the Wironen document which states that “Other factors [followed by a list of substances] . . . or combinations thereof or any other material found to add to the desirable properties of the essential composition of this invention may be included.” Statements of this type recognize that other ingredients have known benefits and may be added to disclosed compositions for their contribution to the composition in question. Therefore, there is a motivation to include the cancellous bone described by Wironen into the O’Leary composition.

Finally, Applicants argue that there are no express teachings for the specific formulations set forth in the claims nor are there any teachings regarding the amounts of cancellous bone to be included. As stated previously, the general amounts of both the demineralized bone matrix and the cellulose material are taught by the references.

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The optimization of the amount of calcium sulfate and mixing solution to be further included is deemed well within the skill of the practitioner at the time the invention was made as it is clear that the amount of calcium sulfate is directly related to desired rate of set up of the composition, i.e. the more calcium sulfate used, the faster the composition will set up and harden. Further, it is clear that the amount of mixing solution is inversely related to the desired set up time and directly proportional to the ultimate consistency of the composition, i.e. the more mixing solution used, the more dilute the calcium sulfate and the slower the set up time but the more liquid the composition will become. Therefore, the Examiner has provided the evidence that optimization is well within the skill of the practitioner. With regard to the cancellous bone, the optimization of amounts is equally within the skill of the practitioner. Wironen discloses the purposes for the inclusion of the cancellous bone in bone implant compositions; therefore, optimization of amounts of cancellous bone to achieve these purposes are deemed also well within the skill of the practitioner. Applicants have provided no evidence of unexpected or surprising results in the use of any given formulation.

In summary, the references, as a whole, certainly provide motivation to add both the calcium sulfate of Yim and the cancellous bone of Wironen to the composition of O'Leary with the expected known and disclosed benefits that both components will add to the composition of O'Leary. O'Leary et al., Yim et al. and Wironen all have the same object in creating a malleable, workable bone growth promoting composition. One of ordinary skill in the art when reviewing the disclosure of Yim would have been

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motivated to include a calcium sulfate component into the composition of O'Leary et al. with the expected benefit disclosed by Yim et al., i.e. that a calcium sulfate component would add improved handling, moldability and consistency to the formulation of O'Leary as well as reducing the set up time. The compositions of Yim and O'Leary are so sufficiently similar that one of ordinary skill in the art at the time the invention was made would be aware of the properties of the calcium sulfate hemihydrate would not impair or otherwise negatively affect the components of the O'Leary composition. Finally, O'Leary et al. teach that other conventional components included in bone growth promoting compositions may be included in the disclosed compositions. Similarly, one of ordinary skill in the art when reviewing the disclosure of Wironen would have been motivated to include a cancellous bone component into the composition of O'Leary with the expected benefit disclosed by Wironen, i.e. that a cancellous bone component would result in improved compositions useful for filling larger bone voids and when these bone chips are not demineralized, they would provide an added spectrum of biological properties not exhibited by the carrier or the carrier plus the osteogenic components.

Conclusion

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

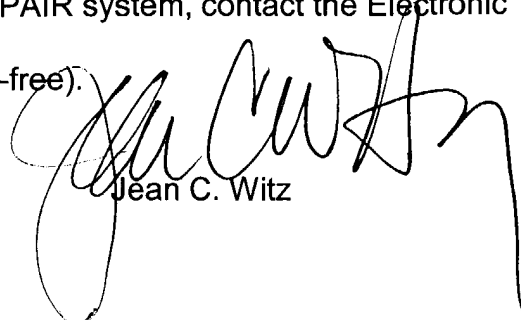
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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (571) 272-0927. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jean C. Witz

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Primary Examiner
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